Remarks

Claims 1-28 were pending in the subject application. By this Amendment, claim 17 has been amended, claims 1-16, 27, and 28 have been cancelled, and new claims 29-46 have been added. Support for the new claims and amendments can be found throughout the subject specification and in the claims as originally filed. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 17-26 and 29-46 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

Applicants note that claim 27, which the Examiner indicated in the July 15 Office Communication as having an incorrect status identifier, has been cancelled by this Amendment and the status of claim 27 indicated as "Cancelled." Applicants respectfully maintain that claim 27, as amended in Applicants' December 14, 2009 Amendment, is directed to the elected invention of Group III. However, in view of the cancellation of claim 27 by this Amendment, the issue is moot.

Claim 17 is objected to on the grounds that it refers back to a withdrawn claim. By this Amendment, Applicants have amended claim 17 to delete the reference back to claim 1 and to specifically recite the text of claim 1 in claim 17. Accordingly, reconsideration and withdrawal of this objection is respectfully requested.

Claims 17-22 and 24-26 are rejected under 35 USC §103(a) as obvious over Petersen (U.S. Patent Publication No. 2002/0094327) in view of Phillips *et al.* (2002) and in further view of Tang *et al.* (2002). In addition, claims 17 and 23 are rejected under 35 USC §103(a) as obvious over Petersen (U.S. Patent Publication No. 2002/0094327) in view of Phillips *et al.* (2002) and Tang *et al.* (2002), further in view of Kovesdi *et al.* (U.S. Patent Publication No. 2003/0027751). The Examiner asserts that the Petersen publication teaches a method of modulating the targeting of pluripotent stem cells to a target tissue of a mammalian subject by increasing the concentration of SDF-1 alpha protein in the target tissue. The Examiner asserts that the Phillips *et al.* publication teaches a vigilant vector comprising a heart-specific promoter (MLC2v) operably linked to a hypoxia response element and a therapeutic gene in an AAV vector, for cardioprotection. The Phillips *et al.* and the Tang *et al.* publications are both cited as teaching a double plasmid approach that produces a powerful chimeric transcription factor consisting of the yeast transcription factor GAL4 DNA binding domain and the

p65 transactivation, that when combined with HRE and SV40 promoter, increased gene expression 400-fold when activated by hypoxia. The Kovesdi *et al.* reference is cited as teaching vectors encoding VEGF administered to cardiac tissue and co-administered with factors (such as GM-CSF) and stem cells. The Examiner concludes that it would have been obvious for a person of ordinary skill in the art at the time of the subject invention to combine the teachings of the cited references and to substitute the SDF-1 alpha gene taught by Petersen for the therapeutic gene of Phillips *et al.* Applicants respectfully traverse these grounds of rejection.

Applicants respectfully assert that the cited references, taken alone or in combination, do not teach or suggest the claimed invention. As the Examiner is aware, in order to support a *prima facie* case of obviousness, a person of ordinary skill in the art must generally find both the suggestion of the claimed invention, and a reasonable expectation of success in making that invention, solely in light of the teachings of the prior art and from the general knowledge in the art. *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). One finds neither the suggestion, nor the reasonable expectation of success, of Applicant's claimed invention in the cited references.

Applicants note that the cited references were all published at about the same time (*i.e.* 2002). However, the Petersen reference does not teach or suggest anything related to the vectors disclosed in the Phillips *et al.* and Tang *et al.* references. If it was so obvious to a skilled artisan to combine the teachings of the cited references, then one would expect that Petersen or another skilled artisan would have published such a disclosure soon after the publication of the cited references, yet the Examiner has not cited any such references. The Phillips *et al.* and Tang *et al.* references may disclose a gene switch for injection directly into the heart. However, the disclosure in the Phillips *et al.* and Tang *et al.* references does not teach or suggest anything regarding stem cells. Thus, Applicants maintain that their claimed invention was not obvious over the cited references.

Applicants respectfully assert that, in addition to the fact that the cited references do not teach or suggest the claimed invention, the cited references also do not provide a reasonable expectation of success in arriving at Applicants' claimed invention. Applicants are the authors of the Phillips *et al.* and Tang *et al.* references and respectfully submit that it took a considerable amount of time and continuous experimentation to conceive and develop the claimed invention. Applicants note that the cited Phillips *et al.* and Tang *et al.* references have a publication date in 2002. The earliest priority

date of the subject application is August 2003. Thus, at least several months of empirical research and development were required by Applicants after the publication of the Phillips *et al.* and Tang *et al.* references in order to arrive at the claimed invention of the subject application.

Applicants respectfully assert that it cannot be predicted that vector systems such as that of the invention will be effective in the intended physiological environment without at least some empirical work providing proof of principle. It was not obvious that an SDF-1 gene could be included in the vector construct of the invention without verifying that the gene could fit in the construct and achieve an effective level of protein expression. The inventors had to empirically determine goodness of fit and the amount of SDF-1 gene expression for a given degree of oxygen deprivation. Furthermore, the inventors had to determine whether tissue-specific promoters were sufficiently powerful to drive expression of SDF-1 so as to be effective *in vivo*. Vector systems must be designed and tested *in vitro* and *in vivo*. As indicated at page 654, second column, of the Phillips *et al.* reference, "basal levels, times of response, tissue specificity, and amplification of signals are all challenges to be met". Moreover, the ability of SDF-1 to attract cardiac stem cells was not known in the art at the time of the present invention, and is particularly advantageous for treatment of cardiovascular pathologies since endogenous cardiac stem cells are probably the most appropriate cell source for use in cardiac repair.

In view of the above remarks, reconsideration and withdrawal of the rejections under 35 USC §103(a) is respectfully requested.

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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